

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (Original): A multiparameter method of screening for the diagnosis, the prevention or the treatment of atherosclerosis-related coronary heart disease (CHD) or stroke comprising;

defining the disease as atherosclerosis-related CHD or stroke;

defining the normal as free from said disease;

defining the following parameters as  
atherosclerotic parameters consisting of  $c$  = the Low-density lipoprotein (LDL) concentration parameter in mg/dL or  $c$  = the C-reactive protein (CRP) concentration parameter in mg/L,  
 $p$  = the blood systolic pressure parameter in mmHg or  $p$  = the blood diastolic pressure parameter in mmHg,  $f$  = the heart rate parameter in  $s^{-1}$ ,  $a$  = the radius parameter along arterial radius in cm,  $T$  = the temperature parameter of

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

blood plasma in °C,  $\alpha$  = the angle parameter between gravity and the mean velocity of blood fluid in arterial vessels in degree and  $z$  = the axial position parameter of diffusion flux along the inner wall in the axial direction of arterial vessels in cm, called the diffusion length;

an individual having the measured values of said atherosclerotic parameters of the following expressions:

$$J = A c^{\frac{11}{9}} (v^3 D^{16})^{\frac{1}{27}} \left( \frac{g \cos \alpha + f u}{z} \right)^{\frac{2}{9}} \quad (1.1)$$

or

$$J = B c^{\frac{11}{9}} p^{\frac{1}{3}} T^{\frac{16}{27}} a^{\frac{2}{3}} f^{\frac{2}{9}} z^{-\frac{2}{9}} \quad (1.2)$$

and

$$J = E c^{\frac{11}{9}} D^{\frac{16}{27}} z^{-\frac{2}{9}} (\cos \alpha)^{\frac{2}{9}} \quad (1.3)$$

wherein  $J$  = the mass transfer flux in  $10^{-5}$  g/(cm<sup>2</sup>s),  $A$ ,  $B$  and  $E$  = the constants of conversion factors,  $v$  = the eddy velocity of blood fluid in arterial vessels in cm/s,  $u$  = the mean velocity of the blood fluid in cm/s,  $D$  = the diffusion coefficient in cm<sup>2</sup>/s, and  $g$  = the gravitational acceleration in cm/s<sup>2</sup>;

the individual having the normal values of said

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

atherosclerotic parameters;

determining the disease risks yielded by the  
differences between said measured values and  
said normal values of said atherosclerotic  
parameters;

adding all said disease risks together yields a  
total risk of said disease;

determining a disease risk level containing said  
total risk of said disease;

selecting an atherosclerotic risk factor related  
to an atherosclerotic parameter that is the  
greatest contribution to said total risk of  
said disease so as to result in said risk  
factor as a primary therapy target of said  
disease;

selecting a greater flux between the LDL mass  
transfer flux and the monocyte mass transfer  
flux so as to result in said greater flux as a  
primary cause in said disease;

selecting a greater concentration level between  
the LDL level in serum and the CRP level in

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

blood plasma so as to result in said greater level as a secondary therapy target of said disease;

determining a relative ratio between currently said total risk and previously said total risk so as to yield said relative ratio as a therapeutic efficacy of said disease;

repeating above-mentioned said methods until said disease risk level is reduced to a normal level for said individual who requires the therapy to prevent or to treat atherosclerosis-related CHD or stroke; and

above-mentioned said methods are written as an executable computer program named the MMA.exe, or another name, to be installed into a general purpose digital computer device to accomplish said methods and to output a result of said methods to a display or a memory or another computer on a network, or to a user.

Claim 2 (currently amended): A method as in claim 1, wherein ~~determining said disease risk yielded by the difference between the measured value and the normal of said LDL concentration parameter~~ the nine

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

disease risks are yielded by the differences between the measured values and the normal values of the nine atherosclerotic parameters, said method comprising the steps of:

a measured value,  $c_m$  in mg/dL, of the individual's LDL concentration in human serum is determined using a medical technique for measuring the concentration of blood constituents or said  $c_m$  is determined by the physician,

a normal value,  $c_n$  in mg/dL, of said LDL concentration is determined by the physician or said  $c_n = 100$  mg/dL for adult,

substituting said  $c_m$  and said  $c_n$  into the following expression where  $c_m \geq c_n$ :

$$R_1 = \left( \frac{c_m}{c_n} \right)^{\frac{11}{9}} - 1 \quad (1)$$

and

calculating (1) yields ~~said~~ the disease risk  $R_1$  caused by ~~said~~ the LDL concentration parameter related to the atherosclerotic risk factors being an elevated LDL concentration in human serum, high-fat diet, hypercholesterolemia or

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

other risk factors that increase said LDL concentration;

a measured value,  $c_m$  in mg/L, of the individual's CRP concentration in human blood plasma is determined using a medical technique for measuring the concentration of blood constituents or said  $c_m$  is determined by the physician,

a normal value,  $c_n$  in mg/L, of said CRP concentration and an equivalent factor,  $F$ , are determined by the physician wherein  $F = \left( \frac{D_c}{D_L} \right)^{\frac{16}{27}}$ ,  $D_c$  = the CRP diffusion coefficient and  $D_L$  = the LDL diffusion coefficient or said  $c_n = 1.0$  mg/L for adult and said  $F = 0.66$ ,

substituting said  $c_m$ , said  $c_n$  and said  $F$  into the following expression where  $c_m \geq c_n$ :

$$R_2 = F \left( \left( \frac{c_m}{c_n} \right)^{\frac{11}{9}} - 1 \right) \quad (2)$$

and

calculating (2) yields the disease risk  $R_2$  caused by the CRP concentration parameter

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

related to the atherosclerotic risk factors  
being an elevated CRP level in human blood  
plasma, systemic inflammation, infectious  
agents or other risk factors that increase said  
CRP level;

a measured value,  $p_m$  in mmHg, of the individual's  
blood systolic pressure is determined using a  
medical technique for measuring the human blood  
pressure or said  $p_m$  is determined by the  
physician,

a normal value,  $p_n$  in mmHg, of said systolic  
pressure is determined by the physician or said  
 $p_n = 120$  mmHg for adult,

substituting said  $p_m$  and said  $p_n$  into the  
following expression where  $p_m \geq p_n$ :

$$R_3 = \left( \frac{p_m}{p_n} \right)^{\frac{1}{3}} - 1 \quad (3)$$

and

calculating (3) yields the disease risk  $R_3$   
caused by the systolic pressure parameter  
related to the atherosclerotic risk factors  
being an elevated level of blood systolic  
pressure, family history of hypertension or

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

other risk factors that increase said systolic pressure;

a measured value,  $p_m$  in mmHg, of the individual's blood diastolic pressure is determined using a medical technique for measuring the human blood pressure or said  $p_m$  is determined by the physician,

a normal value,  $p_n$  in mmHg, of said blood diastolic pressure is determined by the physician or said  $p_n = 70$  mmHg for adult,

substituting said  $p_m$  and said  $p_n$  into the following expression where  $p_m \geq p_n$ :

$$R_4 = \left( \frac{p_m}{p_n} \right)^{\frac{1}{3}} - 1 \quad (4)$$

and

calculating (4) yields the disease risk  $R_4$  caused by the diastolic pressure parameter related to the atherosclerotic risk factors being an elevate level of blood diastolic pressure, family history of hypertension or other risk factors that increase said diastolic pressure;



Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

a measured value,  $f_m$  in  $s^{-1}$ , of the individual's heart rate is determined using a medical technique for measuring the human heart rate or said  $f_m$  is determined by the physician,

a normal value,  $f_n$  in  $s^{-1}$ , of said heart rate is determined by the physician or said  $f_n = 72$  per minute for adult,

substituting said  $f_m$  and said  $f_n$  into the following expression where  $f_m > f_n$ :

$$R_s = \left( \frac{f_m}{f_n} \right)^{\frac{2}{9}} - 1 \quad (5)$$

and

calculating (5) yields the disease risk  $R_s$  caused by the heart rate parameter related to the atherosclerotic risk factors being an elevated level of heart rate, smoking cigarette, depression or other risk factors that increase said heart rate;

a measured radius value,  $a_m$  in cm, of the individual's arterial vessel at the lesion-prone sites of arterial bifurcations, arterial branching, arterial curvatures or arterial tapering is determined using a medical

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

technique for measuring the sizes of arterial vessels or said  $a_m$  is determined by the physician,

a normal value,  $a_n$  in cm, of said arterial radius is determined by the physician or said  $a_n = a$  value between 0.2 cm and 2.2 cm for adult,

substituting said  $a_m$  and said  $a_n$  into the following expression where  $a_m \geq a_n$ :

$$R_6 = \left( \frac{a_m}{a_n} \right)^{\frac{2}{3}} - 1 \quad (6)$$

and

calculating (6) yields the disease risk  $R_6$  caused by the arterial radius parameter related to the atherosclerotic risk factors being an increased size of arterial radius at said lesion-prone sites or other risk factors that increase the size of said arterial radius;

a measured temperature value,  $T_m$  in °C, of the individual's plasma fluid in the region at said lesion-prone sites is determined using a medical technique for measuring the temperature of human blood plasma or said  $T_m$  is determined by the physician,

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

a normal value,  $T_n$  in  $^{\circ}\text{C}$ , of said plasma temperature is determined by the physician or said  $T_n = 37^{\circ}\text{C}$ ,

substituting said  $T_m$  and said  $T_n$  into the following expression where  $T_m \geq T_n$ :

$$R_7 = \left( \frac{T_m}{T_n} \right)^{\frac{16}{27}} - 1 \quad (7)$$

and

calculating (7) yields the disease risk  $R_7$  caused by the plasma temperature parameter related to the atherosclerotic risk factors being an elevated temperature of said human blood plasma at said lesion-prone sites, elevated body temperature-related diseases or other risk factors that increase said plasma temperature;

a measured value,  $\alpha_m$  in degree, of the angle between gravity and the average velocity of the blood fluid in the region at said lesion-prone sites is determined using a medical technique for measuring the human arterial geometries or said  $\alpha_m$  is determined by the physician,

a normal value,  $\alpha_n$  in degree, of said angle is

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

determined by the physician or said  $\alpha_n =$  a value between the 10° and 60° for adult,

substituting said  $\alpha_m$  and said  $\alpha_n$  into the following expression where  $\alpha_n \geq \alpha_m$ :

$$R_8 = \left( \frac{\cos \alpha_m}{\cos \alpha_n} \right)^{\frac{2}{9}} - 1 \quad (8)$$

and

calculating (8) yields the disease risk  $R_8$  caused by the angle parameter related to the atherosclerotic risk factors being a reduced size of said angle or other risk factors that reduce said angle size; and

a measured value,  $z_m$  in cm, of the individual's axial length of diffusion flux along the inner arterial wall at said lesion-prone sites is determined using a medical technique for measuring the human arterial geometries or said  $z_m$  is determined by the physician,

a normal value,  $z_n$  in cm, of said axial length is determined by the physician or said  $z_n =$  a value between 0.10 cm and 1.00 cm,

substituting said  $z_m$  and said  $z_n$  into the

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

following expression where  $z_m \leq z_n$ :

$$R_9 = \left( \frac{z_n}{z_m} \right)^{\frac{2}{9}} - 1 \quad (9)$$

and

calculating (9) yields the disease risk  $R_9$  caused by the diffusion length parameter related to the atherosclerotic risk factors being a decrease in said axial length of the diffusion flux or other risk factors that decrease said diffusion length.

Claim 3-10 (canceled)

Claim 11 (currently amended): ~~A method as in claim 1 having said nine atherosclerotic parameters caused the nine disease risks and~~ The method of claim 2, further comprising: adding said all nine disease risks  $R_1$  to  $R_9$  together so as to yield a total risk of said disease consisting;

a current total risk of said disease related to the currently measured values of said atherosclerotic parameters; and

a previous total risk of said disease related to the previously measured values of said

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

atherosclerotic parameters.

Claim 12 (currently amended): ~~A method as in claim 1 having said total risk of said disease and~~  
The method of claim 11, further comprising:  
determining a disease risk level containing said  
total risk of said disease, ~~said method comprising~~  
~~the steps of:~~

dividing the disease risk level into the  
following seven risk sublevels:  $0.84 \geq$  first  
disease risk level  $\geq 0.00$ ,  $1.75 \geq$  second  
disease risk level  $> 0.84$ ,  $2.70 \geq$  third disease  
risk level  $> 1.75$ ,  $3.70 \geq$  fourth disease risk  
level  $> 2.70$ ,  $4.70 \geq$  fifth disease risk level  $>$   
 $3.70$ ,  $5.80 \geq$  sixth disease risk level  $> 4.70$   
and seventh disease risk level  $> 5.80$ ; and

selecting a disease risk level containing said  
total risk of said disease from among seven of  
said disease risk sublevels.

Claim 13 (currently amended): ~~A method as in claim 1 having said total risk of said disease and~~  
The method of claim 11, further comprising:  
selecting an atherosclerotic risk factor related to

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

the atherosclerotic parameter having the greatest contribution to said total risk of said disease so as to result in said risk factor as a primary therapy target of said disease.

Claim 14 (currently amended): ~~A method as in claim 1 having said LDL concentration parameter caused the disease risk  $R_1$  and said CRP concentration parameter caused the disease risk  $R_2$  and~~ The method of claim 2, further comprising: selecting said a greater flux between the LDL mass transfer flux and the monocyte mass transfer flux so as to result in said greater flux as a primary cause in said disease ~~, said method comprising the steps of:~~

selecting the LDL mass transfer flux as a primary cause in said disease when said  $R_1 \geq$  said  $R_2$ ;  
or

selecting the monocyte mass transfer flux as a primary cause in said disease when said  $R_1 <$  said  $R_2$ .

Claim 15 (currently amended): ~~A method as in claim 1 having said LDL concentration parameter caused the disease risk  $R_1$  and said CRP concentration parameter caused the disease risk  $R_2$  and~~ The method

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

of claim 2, further comprising: selecting said a  
greater concentration level between the LDL level in  
the human serum and the CRP level in the human blood  
plasma so as to result in said greater level as a  
secondary therapy target, ~~said method~~ comprising  
~~the steps of:~~

selecting the LDL level in the serum as a  
secondary therapy target of said disease when  
said  $R_1 \geq$  said  $R_2$ ; or

selecting the CRP level in the plasma as a  
secondary therapy target of said disease when  
said  $R_1 <$  said  $R_2$ .

Claim 16 (currently amended): ~~A method as in~~  
~~claim 1 having said current total risk of said~~  
~~disease and said previous total risk of said disease~~  
~~and determining said~~ The method of claim 11, further  
comprising: determining a relative ratio between said  
current total risk of said disease and said previous  
total risk of said disease so as to yield said  
relative ratio as a therapeutic efficacy of said  
disease.

Claim 17 (canceled)



Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

Claim 18 (currently amended): A method as in claim 1, ~~wherein all the methods in said all processes in claim 1~~ said method has the steps of:

the step 1 of determining the disease risk  $R_1$  yielded by the difference between the measured value  $c_m$  and the normal value  $c_n$  of the LDL concentration parameter wherein  $c_m \geq c_n$  and

$$R_1 = \left( \frac{c_m}{c_n} \right)^{\frac{11}{9}} - 1, \text{ determining the disease risk } R_2$$

yielded by the difference between the measured value  $c_m$  and the normal value  $c_n$  of the CRP concentration parameter wherein  $c_m \geq c_n$  and

$$R_2 = F \left( \left( \frac{c_m}{c_n} \right)^{\frac{11}{9}} - 1 \right) \text{ where } F = \left( \frac{D_c}{D_L} \right)^{\frac{16}{27}}, \text{ } D_c = \text{the CRP}$$

diffusion coefficient and  $D_L$  = the LDL diffusion coefficient, determining the disease risk  $R_3$  yielded by the difference between the measured value  $p_m$  and the normal value  $p_n$  of the blood systolic pressure parameter wherein

$$p_m \geq p_n \text{ and } R_3 = \left( \frac{p_m}{p_n} \right)^{\frac{1}{3}} - 1, \text{ determining the disease}$$

risk  $R_4$  yielded by the difference between the measured value  $p_m$  and the normal value  $p_n$  of the blood diastolic pressure parameter wherein

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

$p_m \geq p_n$  and  $R_4 = \left(\frac{p_m}{p_n}\right)^{\frac{1}{3}} - 1$ , determining the disease

risk  $R_5$  yielded by the difference between the measured value  $f_m$  and the normal value  $f_n$  of the heart rate parameter wherein  $f_m \geq f_n$  and

$R_5 = \left(\frac{f_m}{f_n}\right)^{\frac{2}{9}} - 1$ , determining the disease risk  $R_6$

yielded by the difference between the measured value  $a_m$  and the normal value  $a_n$  of the arterial radius parameter wherein  $a_m \geq a_n$  and

$R_6 = \left(\frac{a_m}{a_n}\right)^{\frac{2}{3}} - 1$ , determining the disease risk  $R_7$

yielded by the difference between the measured value  $T_m$  and the normal value  $T_n$  of the plasma temperature parameter wherein  $T_m \geq T_n$  and

$R_7 = \left(\frac{T_m}{T_n}\right)^{\frac{16}{27}} - 1$ , determining the disease risk  $R_8$

yielded by the difference between the measured value  $\alpha_m$  and the normal value  $\alpha_n$  of the angle

parameter wherein  $\alpha_n \geq \alpha_m$  and  $R_8 = \left(\frac{\cos \alpha_m}{\cos \alpha_n}\right)^{\frac{2}{9}} - 1$ , and

determining the disease risk  $R_9$  yielded by the difference between the measured value  $z_m$  and the normal value  $z_n$  of the diffusion length

parameter wherein  $z_n \geq z_m$  and  $R_9 = \left(\frac{z_n}{z_m}\right)^{\frac{2}{9}} - 1$ ;

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

the step 2 of adding all said nine disease risks  $R_1$  to  $R_9$  in the step 1 together so as to yield a total risk of said disease consisting of a current total risk of said disease related to the currently measured values of the atherosclerotic parameters and a previous total risk of said disease related to the previously measured values of the atherosclerotic parameters;

the step 3 of selecting a disease risk level containing said total risk of said disease in the step 2 from following among seven of the disease risk sublevels:  $0.84 \geq$  first disease risk level  $\geq 0.00$ ,  $1.75 \geq$  second disease risk level  $> 0.84$ ,  $2.70 \geq$  third disease risk level  $> 1.75$ ,  $3.70 \geq$  fourth disease risk level  $> 2.70$ ,  $4.70 \geq$  fifth disease risk level  $> 3.70$ ,  $5.80 \geq$  sixth disease risk level  $> 4.70$  and seventh disease risk level  $> 5.80$ ;

the step 4 of selecting an atherosclerotic risk factor related to an atherosclerotic parameter having the greatest contribution to said total risk of said disease in the step 2 so as to result in said risk factor as a primary therapy

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

target of said disease;

the step 5 of selecting the LDL mass transfer flux as a primary cause in said disease when said  $R_1$  in the step 1  $\geq$  said  $R_2$  in the step 1 or selecting the monocyte mass transfer flux as a primary cause in said disease when said  $R_1 <$  said  $R_2$ ;

the step 6 of selecting the LDL level in human serum as a secondary therapy target of said disease when said  $R_1$  in the step 1  $\geq$  said  $R_2$  in the step 1 or selecting the CRP level in human blood plasma as a secondary therapy target of said disease when said  $R_1 <$  said  $R_2$ ; and

the step 7 of determining a relative ratio between said current total risk of said disease in the step 2 and said previous total risk of said disease in the step 2 so as to yield said relative ratio as a therapeutic efficacy of said disease; and

wherein said step 1 through said step 7 are written as an executable computer program named the MMA.exe, or another name, to be installed into a general purpose digital computer device

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

to accomplish said method and to output a result of said method to a display or a memory or another computer on a network, or to a user comprising:

starting the MMA.exe program on said device;

inputting the currently measured values, the previously measured values and the normal values of the individual's atherosclerosis parameters into the input screen of said MMA.exe by using the keyboard of said device;

clicking the "update" button and the "calc. risk" button of said input screen;

clicking the "evaluate" button of the MMA.exe output screen; and

outputting said output screen to a display or a memory or another computer on a network, or to a user by using said computer device so as to produce a result of said methods, called the screening report containing a total risk of said disease, a disease risk level, a primary cause in said disease, a primary therapy target of said disease, a secondary therapy target of

Appl. No. 10/810,296  
Amdt. Dated Aug. 27, 2007

Reply to Office action of Aug. 22, 2007

said disease and a therapeutic efficiency, to an individual who requires the diagnosis, the prevention or the treatment of atherosclerosis-related CHD or stroke or other cardiovascular disease.

Claim 19 (new): The method of claim 18, further comprising: repeating said method accomplished by using said device until the individual's disease risk level is reduced to a normal level for said individual who requires the therapy to prevent or to treat atherosclerosis-related CHD or stroke or other cardiovascular disease.